increase the dissolution rate (and bioavailability) of a compound, the surface area must increase, thereby decreasing the particle size. The Examiner is also of the opinion that one of ordinary skill in the art would have been motivated to incorporate the particles of Vilkov into the formulation and process of Ayer in order to impart antihistamine properties onto the preparations, and improve dissolution properties. Applicants respectfully disagree.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicants' disclosure.

Section 706.02(j) M.P.E.P. (citing In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)).

In this case, the combination of references cited by the Examiner provides no teaching, suggestion or motivation to produce a dosage form of loratadine having a specific particle size and surface area as claimed by Applicant. Ayer discloses a steroid and a therapeutic composition containing said steroid which is specifically meant for topical or local application for treatment of inflammation of skin. The steroid is ball-milled with a little mineral oil to a particle size of less than 5 microns. It is well known that drug is generally micronized in such topical preparations. Indeed, Ayer lacks any disclosure regarding the reduction of particle size in order to increase the dissolution rate. Ayer only mentions "antihistamines" as one of at least 25 drugs of different classes of therapeutic indications which can be combined with the active steroid.

On the other hand, Vilkov discloses a tablet composition containing pseudoephedrine pellets to provide an extended release, admixed with a tablet mixture containing a second active drug substance selected from amongst various antihistamines that are listed, to provide an immediate release of the drug.

"A single line in prior art reference should not be taken out of context and relied upon with the benefit of hindsight to show obviousness." *Bausch and Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.* 796F.2d 443, 230 USPQ 416 (Fed. Cir. 1986). In this case, Applicants respectfully submit that the Examiner's reliance on one or two incidental sentences in Ayer and a hindsight reconstruction of Applicants' invention fails to set forth a proper *prima facie* rejection. Ayer's mere mention of "antihistamines" as an active ingredient in combination with the active steroid, at best, a tenuous link to the Vilkov disclosure.

Additionally, the emphasis in Vilkov is on the production of a tablet composition for a combination of extended release and an immediate release of two different active ingredients. Applicants respectfully submit that Vilkov's disclosure of a combination of extended release and immediate release provides absolutely no guidance for making a dosage form of loratadine disclosed by Applicants. Applicants further submit that there is no suggestion or motivation in the Vilkov to modify the reference or to combine the reference teachings to make Applicants' invention with a reasonable expectation of success. Thus, the cited references do not render Applicants' invention *prima facie* obvious.

Further, it is clear that neither problem nor its solution is discernible to one with ordinary skill in the art from the teachings of Ayer in view of Vilkov. It is, therefore, felt that the Examiner has failed to make out a *prima facie* case of obviousness and for this reason alone, the obviousness rejection should be overturned. Even if *prima facie* obviousness over Ayer and Vilkov is assumed, the evidence of unexpected and superior results (30% increase

in bioavailability over commercially available formulation of loratadine, Claritin®, see Table 4.2, page 8 and is reproduced below) is sufficient to overcome the *prima facie* case.

Table 4.2

	AUC $_{(0-t)}$	AUC $_{(0-\alpha)}$	C_{max} (μg/ml)
Test/ Reference (%)	134	124	130

For this reason, as well as the arguments presented above, Applicants respectfully request that this rejection be withdrawn.

In light of the foregoing, Applicants believe that this application to be in condition for allowance and respectfully request consideration thereof.

CONCLUSION

For the reasons stated above, the Examiner is urged to pass claims 1-18 to issue immediately. Authorization is hereby given to charge any fees deemed to be due in connection with this Response to Office Action to Deposit Account No. 50-0912.

Respectfully submitted,

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